

REMARKS

Claims 89-127 are pending in the application. Claim 99 has been withdrawn from consideration. Applicants reserve the rights to prosecute the withdrawn subject matter in one or more related applications.

Claims 89 and 90 have been amended to recite an in vitro composition comprising modified cells and unmodified cells of an inbred strain of an animal, and/or the progenies thereof, said modified cells each comprising at least one modification sequence. In claims 89, 90, 93, 94, 95, 113, the recitation of “a plurality of cells” has been amended to recite “a plurality of unmodified cells.”

Claim 93 has also been amended to include the recitation “taken up said targeting DNA construct and.” In claim 98, the term “modified animal cell is a stem cell, a germ cell, or a somatic cell” has been amended to recite “modified cells are stem cells, germ cells, or somatic cells.” In claim 100, the term “modified animal cell” has been amended to recite “modified cells are embryonic stem cells.” Claim 113 has also been amended to recite “and progenies thereof.” In claim 114, the term “modified animal cell” has been amended to recite “modified cells.” In claim 126, the term “modified animal cell produces” has been amended to recite “modified cells produce.” The amendment is fully supported by the originally filed specification and claims. Specifically, the amendment may be found, *inter alia*, at page 2, lines 24 to 33; page 13, lines 10-13; and page 28, line 30 to page 29, line 1. No new matter has been added. Entry of the amendments and the following remarks to the file are respectfully requested.

I. OBJECTIONS TO INFORMALITIES

The Examiner has objected to claims 89-98, 100-127 because of certain informalities. The Examiner alleged that a composition can encompass an animal, which is a non-elected subject matter. Independent claim 89 has been amended to recite “an in vitro composition” and thus do not encompass an animal. Applicants submit that claim 89 and its dependent claims, claims 90-98 and 100-127 are not directed to a non-elected subject matter. As such, objections to these claims have been overcome.

II. REJECTION BASED ON NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 89-98, 100-127 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-23 of U.S. Patent No. 6,653,113 to Berns (“the ‘113 patent”) and claims 1-18 of U.S. Patent No. 5,789,215 (“the ‘215 patent”) to Berns. In response, while not admitting that the claims of the above-identified patent application are not patentably distinct from claims 1-23 of the ‘113 patent or claims 1-18 of the ‘215 patent, Applicants, upon indication of allowable subject matter, will submit a Terminal Disclaimer under 37 C.F.R. § 1.321(c) for the above-identified application.

III. CLAIM REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 89-98, 100-127 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner states that the claims are vague and confusing as they are drawn to the “product by process”. Applicants respectfully disagree. Applicants submit that a product-by-process claim, which is a product claim that defines the claimed product in terms of the process by which it is made, is proper. *In re Luck*, 476 F.2d 650, 177 USPQ 523 (CCPA 1973); *In re Pilkington*, 411 F.2d 1345, 162 USPQ 145 (CCPA 1969); *In re Steppan*, 394 F.2d 1013, 156 USPQ 143 (CCPA 1967).

The Examiner further alleges that the metes and bounds of the claims are indefinite because the product claimed is relative to how or in what way the process is practiced or is relative to the material used. Applicants respectfully disagree.

According to applicable case law, the requirement of 35 U.S.C. § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. Standard Oil Co. v. American Cyanamide Co., 774 F.2d 448, 227 U.S.P.Q. 293 (C.A.F.C. 1985). The test of definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. Orthokinetic Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565, 1 U.S.P.Q.2d 1081 (C.A.F.C. 1986).

In response, claims 89-98, 99-127 have been amended to recite an *in vitro* composition comprising modified cells and unmodified cells of an inbred strain of an animal

and/or the progenies thereof.

Applicants submit that one skilled in the art would appreciate that the claimed compositions of matter are intermediate products formed during various stages of producing a transgenic animal. The present claims are directed to an *in vitro* composition that comprises a heterogenous population of cells which is formed when targeting DNA constructs are introduced into a plurality of cells in a reaction *in vitro*, wherein the plurality of cells and the targeting DNA sequence of the targeting DNA constructs are derived from an inbred strain of animal. In the reaction, some of the cells take up the targeting DNA construct and become modified cells. Those cells that did not take up the targeting DNA construct remain in the reaction as unmodified cells. (Claim 89.) In a certain percentage of the modified cells, the targeting DNA sequence integrate and undergo homologous recombination with the target DNA sequence. (Claims 90, 93-95.) In some other modified cells, the targeting DNA sequence integrate into the genome of the cell without undergoing homologous recombination with the target DNA sequence. These modified cells as well as the unmodified cells in the reaction continue to multiply and produce progenies. Hence, the composition of the present invention comprises both the modified cells and unmodified cells, and their progenies. At a later stage, selection may be applied to the *in vitro* cell composition, which is encompassed in dependent claim 113.

Applicant points out that the claimed *in vitro* cell compositions are clearly described in the specification by way of examples. *See*, page 28, lines 30-37; page 35, lines 20-21 in the specification.

Applicants submit that the claimed *in vitro* cell compositions are each the product of a process, and are defined by how one or more steps of the process are practiced, and the material used. In the specification as filed, the process steps are clearly described and the end points of the process steps are defined. One of ordinary skill in the art would understand from the description how the process steps are carried out and hence, recognize the metes and bounds of the claims. Many elements in the claims are defined in the specification on page 16, line 3 to page 19, line 16 using terms commonly understood by one of ordinary skill in the art of homologous recombination. Moreover, the techniques for introducing DNA into animal cells (claim 112) are well known and clearly described at page 22, line 23 to page 24, line 26 of the filed specification. The materials used in the process are also clearly described at page 19, line 33 to page 22, line 5. e.g., how the targeting DNA is produced (claims 91 and 92); the origins of the cells (claims 96-100; 121-125); the structure and disposition of the

targeting DNA sequence (claims 105-111). The specification also provides guidance on using different materials and process steps (*e.g.*, page 5, lines 5-12; page 7, line 29 to page 8, line 3 of the specification) to achieve different frequencies of homologous recombination resulting in various percentages of modified cells in an *in vitro* cell composition. Methods for determining the percentages of modified cells are well known and described in the specification at page 28, lines 29 to page 29, line 37; page 31, line 10, to page 33, line 2; page 35, line 1 to page 35, line 25; and Table 1.

Applicants submit that the claims in the present invention clearly apprises one of ordinary skill in the art of its scope and therefore, serves the notice function required by the statute. Accordingly, claims 89-98, 100-127 are definite.

IV. CLAIM REJECTIONS UNDER 35 U.S.C. § 102

A. The Rejection under 35 U.S.C. § 102(b) Is In Error

Claims 89-98, 100-127 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Capecchi, 1989, Trends in Genetics, 5(3):70-76 (“Capecchi”). Applicants submit that the rejection is in error.

Applicants disagree with the rejections based on Capecchi since this reference fails to disclose each and every element of independent claim 89 and its dependent claims 90-98, 100-127. The Examiner alleged that since integration of a modifying sequence is not a requirement of claim 89, therefore a progeny does not have to contain a modification to the genome. (Pages 6 and 7 of the Office Action.) Applicants submit that while the progeny of a cell may or may not be modified, however, the invention is not directed to an individual progeny or a final recombinant cell. The claims are directed to an *in vitro* composition of cells, which is made up of a mixed population of cells that are present in different stages of transformation by a targeting DNA construct.

The Examiner further alleged that the claimed and prior art products are identical or substantially identical. Applicants disagree and point out that although Capecchi’s method involves a mixed population of transformed and untransformed cells, the invention is distinguished from the prior art by the fact that the flanking sequences of the targeting DNA construct are derived from the same inbred strain of animal as the cells to which the constructs are targeted. This requirement is nowhere taught in Capecchi. Therefore, since Capecchi does not use the same construct as the present invention, Capecchi could not

possibility teach the mixed cellular composition of the present invention which is created by such construct. Accordingly, Capecchi does not anticipate the present invention.

B. The Rejection under 35 U.S.C. § 102(e) Is In Error

Claims 89-98 and 100-127 have been rejected as being anticipated by U.S. Patent 5,464,764 issued to Capecchi et al. ("the '764 Patent"). Applicants submit that the rejection is in error.

Applicants disagree with the rejections based on the '764 Patent for the same reasons as described above in connection with the Capecchi reference. Accordingly, the '764 Patent does not anticipate the present invention.

CONCLUSION

Entry of the foregoing amendments and consideration of the foregoing remarks are respectfully requested. No fee is believed to be due for this amendment. Should any fee be required, please charge such fee to Jones Day Deposit Account No. 50-3013. Applicants respectfully submit that all claims are now in condition for allowance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining issues.

Respectfully submitted,

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